Ann & Robert H. Lurie Children's Hospital of Chicago
Research Compliance Program Manual

As a leading pediatric research hospital and academic medical center, the Ann & Robert H. Lurie Children's Hospital of Chicago, the Stanley Manne Children's Research Institute, and the Children's Hospital of Chicago Medical Center (the Institution), conducts itself in accordance with the highest level of research ethics in order to protect subjects of research conducted at or sponsored by the Institution. The Institution has developed the following Research Compliance Program in accordance with applicable federal and Illinois State laws, rules, regulations, and guidance governing research, including;

- Office of Research Integrity (ORI) of the Department of Health and Human Services (DHHS)
- Office for Human Research Protections (OHRP)
- Food and Drug Administration (FDA)
- National Institutes of Health (NIH)
- United States Department of Agriculture (USDA)
- Office of Laboratory Animal Welfare (OLAW)
- DHHS Office of Inspector General (OIG)
- Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)

This Research Compliance Program Manual serves as a resource for any person employed by the Institution and its officers, directors, volunteers, researchers, trainees and medical and dental staff (collectively referred to as "staff ") who are involved in research activities. The Research Compliance Program is also intended to cover any other person or organization engaged by the Institution to provide products or services for research. This manual explains the infrastructure of the Research Compliance Program, identifies roles and functions, provides an overview of compliance processes at the Institution, and offers direction about where to find additional, detailed information. The content is intended to complement, not replace, other policies.

With the Research Compliance Program, the Institution will continue to: (a) promote the responsible conduct of research that is fully compliant with the governing regulations, (b) foster an environment that promotes ethical conduct by principal investigators, research personnel and compliance oversight committees, and (c) provide guidance for individual and collective conduct. This Manual is intended to generally define the scope of conduct which the Research Compliance Program is intended to cover but is not intended to be all-inclusive.

The Research Compliance Program aligns with the Institution's Corporate Compliance Program as it sets forth overarching compliance standards across the organization. The Research Compliance Program Manual will be updated periodically to keep personnel informed of and in compliance with a large number of current laws, rules and regulations.

Section 1: Integrity and Research Compliance Program Oversight

A. Director, Office of Research Integrity and Compliance (ORIC)

The Director of ORIC reports to the Chief Operating Officer of the Research Enterprise (COO). The COO serves as the Research Integrity Officer (RIO) and Institutional Official (IO) and retains ultimate responsibility for the supervision and oversight of the Research Integrity and Research Compliance Program. The Director of ORIC oversees matters related to research integrity and provides guidance and oversight to the compliance committees, including but not limited to: the Institutional Review Board (IRB), the Institutional Biosafety Committee (IBC), and the Radiation Safety Committee. The Director works closely with the Legal Department and the Corporate Compliance Office. The Director is responsible for guiding and monitoring compliance activities, maintaining a current knowledge of laws and regulatory requirements, and developing a system whereby related information and updates are disseminated throughout the organization to ensure the Institution is addressing research integrity and research compliance issues. The Director has authority to review all documents and other information that are relevant to research compliance activities.

B. Institutional Review Board (IRB)

The IRB is designated by the Institution to review, approve, and conduct periodic reviews of clinical research studies involving human subjects. The IRB, its membership, and operations are established in conformance with the governing federal regulations and, as required, has a Federalwide Assurance Number. The IRB is subject to audit by the OHRP, ORI, FDA and other governing entities on a routine or 'for cause' basis.

The primary responsibility of the IRB is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating in research. It carefully balances the risks and benefits to ensure the principles of respect for persons, beneficence, justice and equity of selection of research subjects are observed. This is done by reviewing the research plan, informed consent/assent forms, recruitment materials and other related research documents. The IRB typically meets bi-monthly or as deemed necessary.

As the majority of the patients followed at the Institution are children, the IRB is required to follow an additional layer of regulations specific to the protection of children (45 CFR Part 46, Subpart D).

C. Institutional Animal Care and Use Committee (IACUC)

Northwestern University's (NU) IACUC and Center for Comparative Medicine assumed legal authority and responsibility over the Stanley Manne Children's Research Institute (Ann & Robert H. Lurie Children's Hospital of Chicago's) animal care and use program. The regulatory oversight was made effective January 1, 2016, NU's Public Health Service (PHS) Assurance is #A3283-01.

The goal of the IACUC is to ensure the humane care and use of animals used in research, testing and teaching, and that such research is done in accordance with the applicable guidelines and regulations. The IACUC reviews all animal research conducted at the Research Institute to ensure compliance with governing regulations. The review evaluates all aspects of the protocols such as, but not limited to, animal care procedures, animal numbers and justification of animal numbers, husbandry, adequate training and safety precautions of research personnel, research outcomes and endpoints.

The IACUC membership conforms to OLAW requirements. In keeping with the regulations, the IACUC performs semi-annual inspections of the research facility and program review. These reports are submitted to the NU Institutional Official.

D. Institutional Biosafety Committee (IBC)

Institutions conducting research using recombinant DNA are required to follow the *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)*. The Office of Biotechnological Activities (OBA) of the NIH holds each institution's IBC responsible for ensuring that personnel conducting recombinant DNA research follow procedures and practices that are in compliance with the *NIH Guidelines*. The IBC review of recombinant DNA research conducted at the Institution is done when a project is initiated and at least every five years thereafter. The review by the IBC includes areas such as containment levels, training and expertise of research personnel, assessment of facilities, and laboratory safety. The IBC submits an annual report to DHHS/OBA. The IBC meets monthly or more often as deemed necessary.

The Institution's IBC membership complies with the *NIH Guidelines*. The IBC conducts regular laboratory inspections to ensure regulatory and institutional compliance.

E. Compliance Advisory Committee

The Director of ORIC serves on the Compliance Advisory Committee, a multi-disciplinary team that meets regularly and is responsible for implementing the compliance process and ensuring that the appropriate level of compliance activity exists. The Corporate Compliance Officer appoints the members of the committee with advice from leadership and legal counsel.

F. Legal Counsel

The Institution's Legal Department assists the Director of ORIC and other appropriate personnel in identifying and addressing applicable laws, rules, and regulations relevant to the Research Compliance Program. The Legal Department serves as an advisor to the Institution in relation to such laws, rules, and regulations, and assists the Director of ORIC in maintaining the Research Compliance Program in compliance with current laws, rules, and regulations. The Legal Department may review policies and procedures related to the Research Compliance Program to ensure that they adhere to federal, state and other applicable laws, rules and regulations.

The Director of ORIC will notify the Corporate Compliance Office and legal counsel of all reports of material non-compliance, at which time the Director of ORIC and COO, in conjunction and under guidance provided by the Legal Department, will coordinate an investigation of the

reported incident. The Institution will make every effort to preserve and maintain the attorney-client privilege in connection with such investigations, as well as comply with existing and applicable whistleblower protection laws.

G. Corporate Compliance Officer

The Corporate Compliance Officer's oversees the Institution's Corporate Compliance Program.

Section 2: Policies and Procedures and Code of Conduct

The Institution's policies and procedures and Code of Conduct are intended to articulate the commitment to comply with federal, state and other applicable laws, rules and regulations, with an emphasis on preventing fraud and abuse. The Institution is committed to having written policies and procedures in place throughout the organization and providing personnel with access to these while performing their duties. Many of these policies are reviewed regularly by the ORIC. ORIC, in conjunction with the appropriate research compliance committees (i.e., the Institutional Review Board, Institutional Biosafety Committee), will advise affected individuals of any changes and necessary training that will occur as set forth herein.

A. Communication Regarding Integrity and Research Compliance Program

The Research Compliance Program is communicated to principal investigators and research personnel via the Institution's website, global e-mails and training activities (i.e., town hall meetings, post-approval monitoring, etc.). Current research ethics and compliance guidance documents are available on the Institution's internal website. Existing personnel may also receive additional training through their respective departments or the ORIC.

B. Communication Regarding Code of Conduct Guidelines

The Institution has developed the Code of Conduct as a guideline to explain its ethical and legal obligations, and professional conduct standards. The Code is intended to serve as a resource for principal investigators and research personnel and is reinforced through ongoing communication, training and monitoring activities. The Code may be accessed via the Institution's internal website.

C. Conflict of Interest Policies

Issues surrounding conflict of interest or perceived conflict of interest are taken very seriously by the Institution. There are two separate processes addressing conflict of interest. The Policy on Financial Conflict of Interest in Research and Sponsored Programs addresses the issue of conflict of interest for the principal/research investigators and research personnel. The Conflict of Interest Policy for IRB Members addresses conflict of interest affecting the members of compliance review committees (i.e., IRB).

D. Other Policies and Procedures

The Institution also has numerous other policies including; Administrative, Human Resources, Health Insurance Portability and Accountability Act (HIPAA), Occupational Health Services and Emergency.

Section 3: Education and Training

Ongoing education and training is a significant element of the Research Compliance Program. The training program includes, but is not limited to, sessions highlighting the Research Compliance Program and the individual committees, regulatory guidelines governing the conduct of research activities, issues surrounding scientific integrity and misconduct, HIPAA, and any new regulations or guidance issued by the governing bodies. Documentation of formal training undertaken as part of the Research Compliance Program is retained by the ORIC. Each person is held accountable for compliance with all applicable regulations that affect his or her job. All research personnel receive specific training on the regulations and organizational policies and procedures applicable to their job function.

A. Office of Sponsored Programs and Office of Research Integrity and Compliance Outreach Programs

On an ongoing basis, research personnel receive information and training updates on the Research Compliance Program and emerging issues applicable to them. This information is disseminated though the OSP and ORIC departments, through methods including, but not limited to global (institution-wide) email announcements and dedicated training sessions. The staff members of the ORIC and the OSP, under the supervision of their respective Directors, conduct several outreach sessions throughout the year focusing on related policies and procedures, current and proposed regulations and how the Institution ensures compliance.

B. Institutional Review Board

The IRB has specific education requirements for researchers set forth by the federal government. Certification and documentation of completion of the education requirements is a prerequisite for IRB approval of any project. Specific information related to education and training of research personnel is detailed in the IRB Policies and Procedures Manual Section 6: Required Education and Training for Human Subjects Research. IRB members also receive ongoing education regarding research ethics and human subjects' protections through preparation for and discussions at convened meetings.

C. Institutional Animal Care and Use Committee

The IACUC requires that all individuals involved in animal research, teaching, and testing undergo animal training. The NU IACUC Policy and Procedure Manual includes specific information related to education and training of research personnel. In addition, as federally mandated, those individuals who have contact with animals are required to enroll in the Occupational Health and Safety Program.

D. Institutional Biosafety Committee

All Principal Investigators must provide assurance to the IBC that all lab personnel involved conducting recombinant DNA research are trained and are familiar with relevant biosafety practices, protective equipment and techniques, and emergency procedures.

Section 4: Channels of Communication

The Institution believes in an environment of open and candid communications. Research personnel at all levels are encouraged to report in good faith suspected or actual misconduct and any potential violation of law or the Research Compliance Program, so that it can be investigated and properly addressed.

A. Open Door

The Institution has an "open door" policy that permits research personnel to present to management any suspected violation of research ethics or regulatory compliance, the Research Compliance Program, the Conflict of Interest Policy, the Code, or related policies. When reporting a concern about a legal or ethical issue, personnel may choose to first report the concern to their supervisor or to go directly to the Director of ORIC or available senior management. In addition, reports can be made to the Corporate Compliance Office. The Corporate Compliance Office will work in collaboration with the Director of ORIC on research related compliance matters. The Institution will protect, to the fullest extent permitted by law, the identity of personnel who desire to remain anonymous. Personnel who report concerns or suspected problems in good faith can do so without fear of retaliation.

The Institution has also established helplines to encourage personnel to report knowledge or suspicion of illegal or unethical acts. The Institution will protect to the fullest extent permitted by law the identity of callers who desire to remain anonymous and will not tolerate retaliation against individuals who report concerns or suspected problems in good faith.

The phone number to the Institution's Compliance Officer is **312.227.4679**. If personnel prefer to leave a message when reporting a concern they may call the voicemail which is checked daily by the Corporate Compliance Office: **312-227-5288**.

Another option is to call the external Helpline: **1.800.273.8452**. When calling the external Helpline, personnel are greeted by an outside service that will ask for detailed information about their concern. The report will be reviewed with the caller to assure the information is documented accurately and is then forwarded to the Corporate Compliance Office within twenty-four (24) hours of receipt. Callers wanting to remain anonymous will receive an ID number to be used so they can call back to report more details or receive a follow-up response. This Helpline is available twenty-four (24) hours a day, seven (7) days a week.

B. Integrity in Research

It is the policy of the Institution to require high ethical standards in research, and to this end, the Institution takes very seriously any and all allegations of misconduct and/or non-compliance. The ORIC will inquire into, and if necessary, investigate in a timely manner all instances of alleged misconduct.

The Director of ORIC submits an annual report to the ORI of the DHHS regarding any issues of misconduct at the Institution related to human subjects. The ORIC and IRB comply with FDA and

OHRP reporting requirements related to applicable research activities. The IRB Federalwide assurance is updated as required at least every three years.

The NU IACUC, submits annual reports to OLAW, AAALAC, and the USDA regarding animal research activities. The NU PHS Animal Welfare Assurance is updated as required (not less than every five years). Re-registration with the USDA is required every 3 years.

The Director of ORIC, in conjunction with the IBC, and in compliance with *NIH Guidelines*, submits an annual registration and assurance report to the DHHS/OBA.

Section 5: Monitoring and Auditing Systems

The ORIC performs regular auditing and monitoring in order to demonstrate compliance with the Research Compliance Program. Proactive monitoring and auditing functions are designed to verify compliance with legal requirements and with the internal written compliance standards, and federal, state and local laws, regulations and rules. These functions also may assist the Institution in identifying possible misconduct or non-compliance.

A. Internal Reviews

Periodic audits shall be performed to manage high risk areas as identified through communication and/or reports, and as recommended by federal regulatory agencies (e.g. ORI, USDA). Potential areas of audits include, but are not limited to:

1. HIPAA and research requirements.
2. Obtaining and documenting informed consent.
3. Issues surrounding conflicts of interest for researcher and compliance committee board members.
4. Instances of recurrent non-compliance by a specific investigator or department.
5. Issues related to fraudulent research billing charges or misuse of research funds.
6. Approved animal study protocols that involve painful/distressful procedures.

B. Self-disclosure to Government Authorities

Any detected violations of regulations or reportable non-compliance will be reported to the appropriate governing agencies as per the guidelines specified by OHRP, USDA, FDA, NIH, OLAW and ORI. As necessary, the Director of ORIC will consult with legal counsel and the Corporate Compliance Office to ensure appropriate compliance with governing reporting regulations and legal obligations.

Section 6: Enforcement and Discipline

The effectiveness of the Institution's Compliance Program is tied directly to its ability to affect the conduct of each individual in or associated with the Institution. In many instances the Compliance Program's success will be achieved one individual at a time. Building and maintaining meaningful structures of accountability is critical to this effort. When compliance failures occur, there must be a process for enforcing compliance standards and for disciplining responsible individuals when discipline is appropriate. Enforcing standards and disciplining those individuals who violate them emphasizes the Institution's commitment to compliance.

In many instances of research misconduct or serious non-compliance, disciplinary action by the federal government may apply. These actions are public and disseminated in the Federal Register as well as on the ORI website.

Disciplinary action will vary depending on the severity of the offense and such determinations will require the input of legal counsel, Human Resources, ORIC, senior management and research leadership.

A. Failure to Report or Detect an Offense

All employees have a duty to report conduct to the Institution that is unlawful or unethical. Management discusses with employees the compliance policies and legal requirements applicable to their function and explains that strict compliance with these policies and requirements is a condition of employment. Members of management have a duty to report any suspected violations. Failure to adequately instruct personnel or to detect non-compliance, where reasonable diligence on the part of the supervisor should have led to discovery of non-compliance problems, may result in disciplinary procedures for the supervisor and will be reflected in his or her performance evaluation.

B. Reporting False Information

It is a violation of the Compliance Program to knowingly report false information to the Institution or a government agency and there will be consequences for reporting false information (See Section 4 for additional information).

C. Employee Violations

The Institution documents the reasons for disciplinary actions taken against its employees for violations of the Research Compliance Program and related policies. The determination of the appropriate discipline is made in accordance with the Human Resources Disciplinary Action Policy. Disciplinary actions are in proportion to an employee's conduct. Administered discipline is documented in the employee's personnel file. The following factors, among others, may be taken into account by the Institution in determining the appropriate disciplinary action to be imposed for a violation of the Research Compliance Program or related policies:

1. Nature of the violation and the ramifications of the violation for the Institution;
2. Disciplinary action imposed for similar violations;

3. History of past violations;
4. Whether the violation was willful or unintentional;
5. Whether the individual was directly or indirectly involved in the violation;
6. Whether the violation represented an isolated occurrence or a pattern of conduct;
7. If the violation consisted of the failure to supervise another individual who violated the Research Compliance Program or related policies, the extent to which the circumstances reflect lack of diligence;
8. If the violation consisted of retaliation against another individual for reporting a violation or cooperating with an investigation, the nature of such retaliation;
9. Whether the individual in question reported the violation; and
10. Degree to which the individual cooperated with the investigation.

Section 7: Issues Related to Non-Compliance

Issues related to non-compliance with regulations will be managed in order to ensure the protection of human subjects and animals in research. Non-compliance can be the result of actions by the Principal Investigator, research personnel or the compliance committee (e.g. IRB, IACUC and IBC).

The regulations that govern issues related to non-compliance for federally funded research are 45 CFR Part 46 and for FDA regulated research, 21 CFR Parts 50, 56, 312 and 812.

Appendix A: Outlines the processes for reporting, investigating, evaluating and taking action relative to an allegation of non-compliance. The Institution requires the reporting of all types of non-compliance. All reports will be reviewed and evaluated by persons other than the Principal Investigator and research staff.

Non-Compliance

Any of the following actions can be considered non-compliance: (1) the failure to follow the required determinations of the IRB, the NU IACUC, or the IBC; (2) failure to follow their respective policies and procedures; (3) failure to follow the Institution's policies related to the participation of human subjects or animals in research, (4) or failure to follow the applicable regulations.

Range of Non-compliance

The following should be considered when evaluating non-compliance.

- Unintentional to willful
- One time to several times
- Degree of harm to human subjects or animals
- Degree of harm to the integrity of the data

Serious Non-compliance is defined as an action or omission in the conduct or oversight of research that affects the rights and welfare of the subjects, increases the risks to the subjects, decreases the potential benefits or compromises the integrity or validity of the data or research.

Continuing Non-compliance is defined as those incidents of non-compliance that occur more than once representing a pattern of non-compliance.

Principal Investigators, research personnel and anyone else at the Institution (e.g. pharmacy, nursing, etc.) are responsible for reporting any allegations of non-compliance promptly. Reporting can be made to department heads, the appropriate compliance committee (e.g. IRB, IACUC or IBC), research administration, or the Corporate Compliance Office. Patients, sponsors, research subjects, family members or study staff may also report allegations of non-compliance (See Section 4, Part A for additional information).

The ORIC, under the direction of senior management and in consultation with the Corporate Compliance Officer and legal counsel as deemed necessary, may temporarily suspend the research pending the outcome of the inquiry or investigation; may permit research to continue during the inquiry or investigation; may require modification to the research as a condition for the research; and may require additional education and training for research staff and the investigator. The Corporate Compliance Office will be made aware of final decisions around non-compliance.

Non-compliance of the Institutional Review Board, the Institutional Animal Care and Use Committee or the Institutional Biosafety Committee

Non-compliance by one of the committee includes, but is not limited to, meetings held without a quorum, research reviewed without the appropriate expertise, block voting on proposals or voting by members with a conflict of interest.

The committee chair may be found to be in non-compliance should the chair not manage the meeting to allow for adequate discussion and deliberation of proposals, if the members do not follow the applicable regulations in reviewing the research, and if minutes do not appropriately reflect the decisions and determinations of the committee.

Institutional Review Board

For policies specific to the managing and reporting of non-compliance in the conduct of research of human subjects, please see the IRB Policies and Procedures Manual.

Section 8: Investigation, Response and Prevention

The term “investigation” is often used to describe the various responses the Institution might take to address known or suspected misconduct. Depending on the circumstances involved in the incidence, an investigation may be merely an informal inquiry, or it may involve more formal steps such as a detailed audit of research records. In addition to other preventative measures, an effective response to identified research non-compliance will include appropriate monitoring of ongoing activities to assure that corrective and preventative measures are effective in eliminating recurrences of the non-compliance.

A. Investigation of Reported Violations

The Director of ORIC initiates investigations of reported violations, implements corrective action, and will take the necessary steps to secure or prevent the destruction of documents or other evidence relevant to the investigation.

The Director of ORIC consults with legal counsel and the Corporate Compliance Office regarding the manner in which to respond to a report (e.g., internally or externally directed investigations required disclosures or actions to be taken in response to a report of a violation of the Research Compliance Program or related policies). To the extent permitted by law, and in order to protect the reputation of those involved, the confidentiality and identity of the parties will be respected.

Upon receipt of reports of reasonable indications of suspected non-compliance, the ORIC will promptly assess the conduct in question to determine whether a material violation of applicable law or Research Compliance Program has occurred. Instances of non-compliance are evaluated on a case-by-case basis. The internal investigation may include interviews and a review of relevant documents. As appropriate, records of the investigation should contain documentation of the alleged violation, a description of the investigative process (including objectivity of investigators and methodologies utilized), key documents, a log of witnesses interviewed and the corrective action taken. Retention of records related to the investigation will be in accordance with applicable regulations.

The ORIC, under the direction of senior management, reserves the right to remove the person(s) under investigation, or the person(s) allegedly involved in the misconduct from current work activity until the investigation is completed.

B. Corrective Action

The Institution responds quickly and appropriately to all reported violations. ORIC policies and procedures may be modified to guard against further violations. All violations of law, regulations or policies are processed through established disciplinary procedures.

Should the investigation reveal that there is systemic non-compliance, the Director of ORIC may consult with legal counsel and the Corporate Compliance Officer, and others as deemed appropriate, to determine: (a) the corrective action the Institution should take, if any, and (b) whether or not the Research Compliance Program and related policies should be modified to address such non-compliance.

C. Government Audits and Investigations

Government agencies such as the OHRP, the FDA, or the USDA may conduct audits of the compliance committees at any time. These audits may be "for cause," (where there is reasonable belief on the part of the agency that there is evidence of non-compliance), or they may be routine in nature (scheduled visits at regular intervals) to assess current practices. If any government entity institutes an investigation, ORIC will immediately inform the Corporate Compliance Officer and will inform the COO/RIO of the Research Institute and research leadership, relevant Compliance Committee Chairs, the ORIC staff, and other support services as necessary (e.g. research pharmacy, the CRO, etc.). If such an investigation occurs, legal counsel will be notified and may inform research personnel of their rights and obligations with respect to requests for interviews from governmental investigators.

Any Principal Investigator who is contacted by a research sponsor or regulatory agency regarding an audit or investigation should notify the ORIC which is able provide guidance, support, and any necessary regulatory documentation related to the research activities.

Staff members should refer any contact from a government official regarding an investigation or inquiry to the Director of ORIC. The Corporate Compliance Office will also be made aware of any investigations.

Section 9: Updates & Modifications

The Director of ORIC, under the guidance of the COO/RIO and advice of the Corporate Compliance Office, will review the Research Compliance Program to determine if revisions and/or updates are necessary to address new issues encountered in their administration, the enactment of new laws and/or the promulgation of new regulations, or other relevant changes.

The COO/RIO and the Chief Research Officer of the Institution will approve all amendments and modifications to the Research Compliance Program.

DISCLAIMER

This Research Compliance Program is not intended to and does not create contract rights in any person. It is informational in nature and is used by the Institution to guide it in the exercise of its discretion. It is subject to change or revocation without prior notice.

APPENDIX A:
Office of Research Integrity and Compliance
Policy on Research Integrity and Procedures for Reviewing Allegations of Misconduct

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A. Statement of Principles

This section provides a statement on integrity in research; describes the responsibilities of research personnel, administrators, and others at the Institution; and sets forth the procedures to timely, effectively and fairly respond to allegations of research misconduct.

Maintaining high ethical standards in the conduct of scientific research is an important responsibility imposed by public trust and is essential to the discovery of new knowledge and the reputation of research, researchers and research institutions. Misconduct or apparent misconduct in scientific research challenges the integrity of the scientific enterprise at large and threatens to undermine public trust in research.

It is the policy of the Institution to require high ethical standards in research; to inquire into and, if necessary, to investigate and resolve promptly and fairly all instances of alleged misconduct; to comply in a timely manner with agency requirements for reporting on cases of possible misconduct when sponsored project funds are involved; and to provide full and continuing cooperation with granting agencies during their oversight review under this policy and applicable federal regulations. This section offers explicit and official procedures necessary to assure that allegations of research misconduct are properly addressed and to promote ethical standards in scientific research and dealing with alleged misconduct.

Because a charge of misconduct, even if unjustified, may damage an individual's career, any such issue must be handled in a prudent and confidential manner. To help protect the confidentiality of respondents, complainants and witnesses, all disclosures identifying these persons should be limited to those who have a need to know the information consistent with a thorough, competent, objective and fair research misconduct proceeding. Also, an inquiry or investigation must be handled promptly and expeditiously with full attention given to the rights of all individuals involved.

The review process for determining whether research misconduct has occurred and for providing corrective actions consists of three phases: inquiry, investigation, and adjudication. The goal of these procedures is to ensure fair treatment for each person alleged to have committed an act of research misconduct. Therefore, every inquiry and subsequent investigation will be based on a presumption of innocence until proven otherwise. It is not intended that the proceedings be adversarial. Rather, all phases of the procedure should be conducted in the spirit of peer review.

B. Applicability

The Research Compliance Program policies applies to all persons affiliated with the Institution, whether the research is funded or not, and is applicable to physicians, fellows, residents, students, and all other members of the research staff. Cases of research misconduct involving residents and students are subject to the normal disciplinary rules governing residents and students, but may be reviewed, as appropriate, under the Institution's Compliance Program.

The Research Compliance Program policies apply to: the conduct of extramural and intramural biomedical or behavioral research or activities related to that research, the conduct of biomedical or behavioral research training programs or activities related to that research training, contracts and other forms of support, regardless of source, grants, procurement contracts and cooperative agreements, the presentation or publication of results, the process of applying for funds, and the expenditure or fiscal reporting on the use of project funds.

The Research Compliance Program policies also apply to any research proposed, performed, reviewed, or reported, or any research record generated from that research, regardless of whether the user or reviewer receives federal support or whether an application or proposal for federal funds resulted in a grant, contract, cooperative agreement, or other form of federal support. Research misconduct proceedings involving federally-supported research shall be conducted in accordance with all applicable federal policies and regulations. Research misconduct proceedings not involving federally-supported research shall be guided by those same principles.

2. DEFINITIONS

Abuse of Confidentiality means the use of ideas and preliminary data gained from (i) access to information not otherwise available through the opportunity for editorial review of manuscripts submitted to journals, and (ii) the opportunity for peer review of proposals being considered for funding by agency panels or by internal committees such as the Institutional Review Board, the Institutional Animal Care and Use Committee, or the Radiation Safety Committee.

Allegation is a disclosure of possible Research Misconduct through any means of communication. The disclosure may be by written or oral statement or other communication to an institutional or HHS official.

Complainant is the person(s) who in *Good Faith* makes an *Allegation* of *Research Misconduct*.

Deciding Officer is the Chief Research Officer who serves as the Deciding Officer for the purposes of this policy.

Evidence means any document, tangible item, or testimony offered or obtained during a research misconduct proceeding that tends to prove or disprove the existence of an alleged fact.

Fabrication is making up data or results and recording or reporting them.

Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.

Good Faith means having a belief in the truth of one's allegation or testimony that a reasonable person in the Complainant's or witness's position could have based on the information known to the Complainant or witness at the time. An allegation or cooperation with a research misconduct proceeding is not in good faith if made with knowing or reckless disregard for information that would negate the allegation or testimony.

Inquiry is the preliminary information-gathering and preliminary fact-finding to determine whether an allegation or apparent instance of research misconduct has substance and if an investigation is warranted.

Investigation is the formal development of a factual record and the examination of that record leading to a decision not to make a finding of research misconduct or to a recommendation for a finding of research misconduct or other appropriate remedies, including administrative actions.

Preponderance of the Evidence means the proof by information that, compared with that opposing it, leads to the conclusion that the fact at issue is more probably true than not.

Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

Research means a systematic experiment, study, evaluation, demonstration or survey designed to develop or contribute to general knowledge (basic research) or specific knowledge (applied research) relating broadly to public health by establishing, discovering, developing, elucidating or confirming information about, or the underlying mechanism relating to, biological causes, functions or effects, disease treatments, or related matters to be studied.

Research Integrity Officer is the COO of the Research Institute or another person with sufficient knowledge and experience to handle the procedural and regulatory requirements person who is appointed by the Chief Research Officer to serve as the Research Integrity Officer (RIO).

Research Misconduct is *fabrication*, *falsification*, or *plagiarism* in proposing, performing, or reviewing research, or in reporting research results. It also includes *abuse of confidentiality*. Research misconduct does not include honest error or honest differences of opinion.

Research Record is the record of data or results that embody the facts resulting from scientific Inquiry, including but not limited to, research proposals, laboratory records, both physical and electronic, progress reports, abstracts, theses, oral presentations, internal reports, journal articles, and any documents and materials provided to HHS or an institutional official by a respondent in the course of the research misconduct proceeding.

Respondent is the person(s) against whom an allegation of research misconduct is directed or who is the subject of a research misconduct proceeding.

Retaliation means an adverse action taken against a complainant, witness, or committee member by an institution or one of its members in response to (a) a good faith allegation of research misconduct; or (b) good faith cooperation with a research misconduct proceeding.

3. RESPONSIBILITIES

A. Principal Investigators and Research Personnel. Principal Investigators and research personnel are responsible for maintaining the highest ethical standards in their research.

Principal Investigators are responsible for:

(1) assuring that these standards are communicated to and maintained by all who work under their supervision, directly or indirectly,

(2) assuring the validity of all information communicated by their research personnel, and

(3) Assuring adequate citation of contributions from those within and without each research group. Co-authorship should reflect scientific involvement and responsibility for work reported. Although collaborative relationships between investigators are based on trust, some joint evaluation of data should be an integral part of the review process, even when unique laboratory procedures necessitate long-distance collaboration.

B. Administrators. The COO/RIO and the Director of ORIC are responsible for the implementation and updating of the Research Compliance Program. They will assure widespread dissemination, posting to the Institution's internal website, and that appropriate review procedures are promptly implemented when allegations of research misconduct are reported. The Chief Research Officer will be notified of all inquiries and investigations and their outcome. Accurate records will be maintained and, where required, proper and timely reporting to relevant agencies will be made for any determinations of research misconduct which the Institution must report. The Chief Research Officer represents the Institution when it is determined that present or former research personnel are the subject of complaints or investigations that involve outside institutions. In the event of a

determination of research misconduct, the Chief Research Officer may invoke sanctions according to established Institutional procedures.

C. Members of the Medical Center Community. Members of the medical center community are responsible for reporting what they believe to be research misconduct on the part of research personnel. To the extent consistent with the needs of an inquiry or investigation, the identity of confidential sources will be protected. Those who provide information in good faith about questionable conduct will be protected against retaliation.

4. PROCEDURES FOR REVIEWING RESEARCH MISCONDUCT

A. Reporting Allegations

(1) Reports of alleged research misconduct on the part of employees or persons within the control of the Institution are to be made by written or oral statement or other communication directly to the appropriate department head, who will immediately inform the COO/RIO of the substance of the allegations. Complaints that relate to Institution's research programs, involve more than one department, or by their nature require special consideration (e.g., cases brought by or against a department head) may be addressed directly to the COO/RIO, who will then notify the Institution's President and the Chief Research Officer about the allegation and thereafter of its disposition. Generally, the alleged research misconduct must have occurred within six (6) years of the date the allegation is reported to an institution or HHS.

(2) The Institution must, either before or when the Institution notifies the respondent of the allegation, inquiry or investigation, promptly take all reasonable and practical efforts to obtain custody of all the research records and evidence needed to conduct the research misconduct proceeding and sequester them in a secure manner. Reasonable accommodations for access to data or copies of sequestered records will be made when necessary and appropriate.

(3) A preliminary and informational evaluation of the complaint will be made by COO/RIO, who may consult in confidence with others as appropriate before passing on the matter.

(4) If the COO/RIO finds there is no sufficiently credible and specific evidence supporting the research misconduct allegation, and the Chief Research Officer concurs, the complaint will be dismissed without giving any notice to the respondent. A written report stating the reasons for the dismissal shall be maintained, but will not be made a part of the records of the respondent. The complainant, who shall be notified of the dismissal, may

appeal a decision for dismissal directly to the Chief Research Officer or to the Institution's President. If the complaint is not dismissed, then an inquiry will be conducted.

(5) If, after evaluation, the COO/RIO believes an allegation describes an instance of research misconduct and is sufficiently credible and specific so that potential evidence of research misconduct may be identified, the COO/RIO shall refer the case directly to the Chief Research Officer for inquiry. In either event, the respondent shall be notified in writing of the allegation and shall be given a copy of the procedures for review of research misconduct. Individuals with supervisory responsibility for the respondent will also be notified as appropriate.

B. Inquiry

(1) The purpose of an inquiry is to determine whether an allegation or apparent instance of research misconduct warrants a full investigation or requires that special action be taken pending resolution of the allegation or apparent misconduct. The inquiry will determine whether the allegation of research misconduct appears to be well-founded, the seriousness of the alleged misconduct, the scope of the alleged incident, and the relevance of any other information that is available. Because an inquiry is an initial review, it does not require a full review of all of the evidence related to the allegation. An inquiry should be completed within sixty (60) calendar days after an allegation is made.

(2) To the extent possible, inquiries (and resultant investigations) will be conducted in a confidential manner so as to protect the affected parties. Although a person participating directly in the conduct of an inquiry or investigation must be qualified to evaluate the situation, no such person may have unresolved, personal, professional, or financial conflicts of interest with the complainant, respondent or witnesses.

(3) If an inquiry is made, the Chief Research Officer will appoint an ad hoc committee of at least three (3) full-time staff members, and the same procedures for inquiry will be followed. Additionally, the COO/RIO shall serve as a non-voting staff member of the inquiry committee.

(4) The Chief Research Officer shall abide by any applicable protocols for appropriate custody and maintenance of all the research records and evidence needed to conduct the research misconduct proceeding.

(5) The inquiry committee will review the merits of the Allegations and recommend a course of action to the Chief Research Officer, as appropriate, including whether a full investigation should be conducted.

The committee may have access to documents relating to the alleged misconduct and may interview the complainant, respondent and any relevant witnesses. It shall not, however, attempt to reach a decision on the merits of the complaint. The committee shall prepare a written inquiry report that states what evidence was reviewed, summarizes relevant interviews, and includes the conclusions of the inquiry.

(6) After receiving the written report of the inquiry committee, the committee will forward a copy of its report, along with its recommendations, to the Chief Research Officer, the department head, and to the respondent. The respondent may make written comments to the Chief Research Officer. The Chief Research Officer will determine whether to dismiss the case or to proceed with an investigation. The respondent and the division chair, if applicable, and department chair will be notified in writing of the decision of the Chief Research Officer.

(7) If the complainant disagrees with a decision of the Chief Research Officer to dismiss the case, the complainant may appeal to the Institution's President. A notice of appeal should also be provided to the respondent. The Institution's President then will review the case and make a final determination as to appropriate action.

(8) If a decision not to investigate is rendered, all the information assembled in the course of the inquiry will be maintained in confidence for at least seven (7) years to permit a later assessment of the reason for determining that an investigation was not warranted. See also Section D.2 for certain notification requirements that may be applicable.

(9) If the inquiry concludes that there appears to be grounds for a charge of research misconduct, the Chief Research Officer will initiate a formal investigation into the matter in accordance with Section C. The Institution's President and the respondent must be notified of the decision to commence a formal investigation. If the matter involves federally supported research or an application for federal support, the ORI will also be notified in the time and manner required by federal regulations.

C. Investigation

(1) The purpose of an investigation is to examine thoroughly in an unbiased, impartial manner, an allegation of research misconduct and to determine whether such misconduct has taken place. A finding of research misconduct that there be a significant departure from accepted practices of the relevant research community, that the misconduct be committed

intentionally, knowingly, or recklessly and that evidentiary standards are satisfied.

Evidentiary Standards:

Burden of Proof: The Institution has the burden of proof for making a finding of research misconduct. The respondent has the burden of proof as to any affirmative defenses and mitigating factors. However, destruction of research records or respondent's failure to furnish research records adequately documenting the questioned research, establishes a rebuttable presumption of research misconduct that may be relied upon by the Institution.

Standard of Proof: A determination that research misconduct has occurred must be established by a preponderance of the evidence.

(2) If the Chief Research Officer determination is to proceed with an investigation, he will appoint a committee of full-time staff members without any unresolved, personal, professional, or financial conflicts of interest with the complainant, respondent or witnesses to investigate the complaint and will notify the respondent within a reasonable time but before the investigation begins. If not already performed, the Institution must take custody of the records before or concurrently with the notification of the respondent. The complainant is not a party to the misconduct proceeding, but rather acts as a witness after the allegation is made. When appropriate, the Chief Research Officer may appoint experts who are not full-time clinical staff members of the Institution to serve on the committee. Granting agencies supporting the research work under investigation will be notified by the Chief Research Officer that an investigation is taking place, as may be required by the agency. Specific agency requirements, such as the time within which certain steps are to be taken will be observed and will be communicated by the Chief Research Officer to the investigating committee and to the respondent. For example, PHS guidelines require that an investigation start within thirty (30) days of completion of an inquiry and that the investigation concludes within one hundred twenty (120) days, unless permission for extension is granted by the relevant funding agency.

(3) The investigation will include, but not be limited to, review of grant or contract files, reports, scholarly publications, manuscripts, and other documents; inspection of laboratory or clinical facilities and/or materials; interviewing of parties with an involvement in or knowledge about the case; and submission of a formal report of committee findings, including response of the respondent.

(4) The respondent will be kept informed by the investigatory committee chairperson of the general progress of the investigation, and will be given the opportunity to respond to the complainant orally and in writing and to provide information for consideration by the committee.

(5) The investigatory committee will focus on matters limited to the charge given to it by the Chief Research Officer, but may review previous research efforts of the affected personnel, or records of previous complaints of research misconduct, if germane to the investigation.

(6) Neither the Institution, nor the respondent may have legal counsel present at the meetings, except at the express invitation of the committee. Should legal counsel be invited, the invitation will be extended to both parties. When invited, legal counsel may observe but shall not participate in the proceedings. With the prior approval of the investigatory committee, the respondent may be accompanied by a non-attorney colleague.

(7) The investigatory committee will prepare a draft final report and provide a copy of such report to the respondent, who may review and comment, offer corrections, accept its conclusions, or deny the allegations within thirty (30) days of receipt. The investigatory committee will then compile the final report and will transmit it to the Chief Research Officer along with any minority reports and responses by the respondent. The committee's report will respond to the charge given by the Chief Research Officer, will assess the validity of the allegations of misconduct and will recommend sanctions or other action.

(8) The report of the committee and its attachments along with the recommendations of the Chief Research Officer will be forwarded to the Institution's President for review and disposition. If the Institution's President finds that the respondent has not engaged in research misconduct, the President will dismiss the complaint. If the President finds that the respondent has engaged in research misconduct, the President may order appropriate sanctions and may initiate procedures leading to possible additional sanctions. The President will inform the respondent, the Chief Research Officer, the department head, and the division chair of their decision.

D. Adjudication

(1) At the conclusion of the investigation, or at any other time required by an involved granting agency, the Chief Research Officer will notify the granting agency of the facts of the case, the conclusions rendered, and the disposition of the matter by the Institution. The Chief Research Officer will

notify other outside parties as may be appropriate, including publishers or institutions with whom the party found to have committed research misconduct is now or has been professionally affiliated. The Institution's President will consider release of information about the incidence to the public.

(2) For PHS-supported research, the Chief Research Officer must carry inquiries and investigations through to completion and pursue diligently all significant issues. The Chief Research Officer must notify ORI in advance if the Institution's plans to close a case at the inquiry, Investigation, or appeal stage on the basis that the respondent has admitted guilt, a settlement with the respondent has been reached, or for any other reason. The Chief Research Officer need not report to ORI the closing of a case at the inquiry stage on the basis that an investigation is not warranted. The Chief Research Officer must report a finding of no misconduct at the investigation stage, but this need not occur in advance of the decision.

(3) If the alleged misconduct is not substantiated by the Investigation, diligent efforts will be made to restore fully the reputation of the respondent. In addition, all reasonable and practical efforts will be made to protect or restore the position and reputation of any complainant, witness or committee member and to counter potential or actual retaliation against them. However, if it is further demonstrated that the charges were brought under malicious or dishonest circumstances, then the Institution's President may bring appropriate action against the complainant or others involved.

(4) A permanent record of committee reports, exhibits, minutes of meetings, and other materials will be kept by the Chief Research Officer for 7 years after the completion of any PHS proceeding involving the research misconduct allegations. These records will be protected from release, if release would compromise the conduct of an investigation, constitute unwarranted invasion of privacy, or reveal the content of communications or recommendations of action to be taken. In the case of sponsored projects, the Chief Research Officer is responsible for determining and complying with reporting requirements; representing the Institution in all negotiations with the sponsor; and implementing any administrative actions that may be directed by the sponsor.

(5) Consistent with procedures described above, those responsible for the conduct of inquiries and Investigations shall have at any time the authority to supplement and clarify applicable procedures, provided that adequate notice is given to persons affected by such actions.

(6) The Chief Research Officer or the Institution's President may take action, and notify ORI, without prior hearing or review should either of them conclude that any of the following conditions exist:

(a) The health or safety of the public is at risk, including an immediate need to protect human or animal subjects;
(b) HHS resources or interests are threatened
(c) Research activities should be suspended
(d) There is a reasonable indication of possible violation of civil or criminal law;
(e) Federal action is required to protect the interest of those involved in the research misconduct proceeding;
(f) The Chief Research Officer or the Institution's President believe the research misconduct proceeding may be made public prematurely so that HHS may take appropriate steps to safeguard evidence and protect the rights of those involved; or
(g) The research community or public should be informed

SOURCE:
70 Federal Register 28369 (May 17, 2005) (Public Health Service Policies on Research Misconduct Final Rule).

Exhibit A:
Protocol for Custody of Records
Record Retention and Custody of the Research Misconduct Proceeding

Once the Institution undertakes any actions related to alleged research misconduct including allegation assessment, inquiries, investigations, or ORI oversight reviews, the Institution must promptly take all reasonable and practical steps to obtain custody of all the research records and evidence needed to conduct the research misconduct proceeding, inventory the records and evidence, and sequester them in a secure manner.

Records of the research misconduct proceeding that must be taken into custody include:

- The records that the Institution secures for the proceeding, except to the extent the research center subsequently determines and documents that those records are not relevant to the proceeding or that the records duplicate other records that are being retained;
- The documentation of the determination of irrelevant or duplicate records;
- The inquiry report and final documents (not drafts) produced in the course of preparing that report, including the documentation of any decision not to investigate;
- The investigation report and all records (other than drafts of the report) in support of that report, including the recordings or transcriptions of each interview (version after interviewee is given opportunity to correct); and
- The complete record of any Institutional appeal, if provided.

Maintenance of Records

Unless custody has been transferred to HHS, or ORI has advised the Institution in writing that it no longer needs to retain the records, the Institution will maintain all records of the research misconduct proceeding identified above in a secure manner for seven (7) years after completion of the proceeding or the completion of any PHS proceeding involving the research misconduct allegation, whichever is later.

Provision for HHS custody

On request, the Institution must transfer custody of or provide copies to HHS, of any Institutional record relevant to a research misconduct allegation, including the research records and evidence, to perform forensic or other analyses or as otherwise needed to conduct an HHS inquiry or investigation, or for ORI to conduct its review or to present evidence in any proceeding.

SOURCE: 70 Federal Register 28,369 (May 17, 2005) (Public Health Service Policies on Research Misconduct Final Rule).

Exhibit B:
Protocol for Inquiry Report
Drafting the Inquiry Report

Within 30 days of finding that an investigation is warranted, the Institution must provide ORI with the written finding by the Chief Research Officer and a copy of the inquiry report. The inquiry report must be in writing and include:

- The name and position of the respondent;
- A description of the allegations of research misconduct;
- The PHS support, including, for example, grant numbers, grant applications, contracts, and publications listing PHS support;
- The basis for recommending that the alleged actions warrant an investigation;
- And, any comments on the report by the respondent or the complainant.

The Institution must have the following information and documentations ready and available to provide to ORI upon request:

- The Institution's policies and procedures under which the inquiry was conducted;
- The research records and evidence reviewed, transcripts or recordings of any interviews, and copies of all relevant documents; and
- The charges for the investigation to consider.

If the Institution makes a finding that an investigation is not warranted, then the Institution must keep sufficiently detailed documentation of the inquiry to permit a later assessment by ORI of the reasons why the Institution has decided not to conduct an investigation.

Consistent with the Custody of Records Protocol, the Institution must keep these records in a secure manner for at least seven (7) years after the termination of the inquiry, and upon request, provide them to ORI or other authorized HHS personnel.

SOURCE: 70 Federal Register 28,369 (May 17, 2005) (Public Health Service Policies on Research Misconduct Final Rule).

Exhibit C:
Protocol for Investigation Report
Drafting the Investigation Report

Within 120 days of initiating the investigation of research misconduct, the Institution must provide ORI with the Final Institutional Investigation Report prepared by the Chief Research Officer. The investigation report must be in writing and include:

- A description of the nature of the allegations of research misconduct;
- A description of the PHS support, including, for example, any grant numbers, grant applications, contracts, and publications listing PHS support;
- A description of the specific allegations of research misconduct for consideration in the investigation;
- A copy of the institutional policies and procedures under which the Investigation was conducted, (if not already provided to ORI with the inquiry report);
- Identification and summary of the research records and evidence reviewed, and identification of any evidence taken into custody but not reviewed;
- For each separate allegation of research misconduct identified during the investigation, provision of a finding as to whether research misconduct did or did not occur, and if so -
    - Identification of whether the research misconduct was falsification, fabrication, or plagiarism, and if it was intentional, knowing, or in reckless disregard;
    - Summary the facts and the analysis which support the conclusion and consider the merits of any reasonable explanation by the respondent;
    - Identification of the specific PHS support;
    - Identification of whether any publications need correction or retraction;
    - Identification of the person(s) responsible for the research misconduct;
    - And, listing of any current support or known applications or proposals for support that the respondent has pending with non-PHS Federal agencies

SOURCE: 70 Federal Register 28,369 (May 17, 2005) (Public Health Service Policies on Research Misconduct Final Rule).